

Prevention of Sudden Death With the Implantable Defibrillator in Hypertrophic Cardiomyopathy

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Hypertrophic cardiomyopathy (HCM) is the most common cause of sudden cardiac death in the young, including competitive athletes.¹⁻⁴ Indeed, the predisposition of patients with this complex form of genetic heart disease to arrhythmic risks has been known from the time of its modern recognition, almost 50 years ago.⁵ For much of this time, efforts to protect patients with HCM from sudden death focused on pharmacologic strategies (including amiodarone, beta-blockers, and type IA antiarrhythmic agents) and were largely unsuccessful.^{1,2}

More recently attention has turned to the implantable cardioverter-defibrillator (ICD) as the most effective preventive therapy against sudden death, both in survivors of cardiac arrest and prophylactically in high risk patients.⁶

Background

The ICD represents one of the major advances in cardiovascular medicine in the last 100 years.⁷ For the past 25 years the ICD has been used with increasing frequency for the prevention of sudden death, saving

and prolonging the lives of thousands of patients largely with coronary artery disease and heart failure.^{7,8}

The cardiovascular community has been slow to adopt and translate this powerful therapeutic strategy to genetic heart diseases, which nevertheless are responsible for most of the sudden deaths in youthful and middle-aged patients.^{1,2,4} Indeed, it was not until the year 2000 that data reported from a large group of patients with HCM promoted the efficacy of the ICD for this disease.⁶ Importantly, that publication triggered greater numbers of implants in the HCM patient population,^{9,10} as well as in the other genetic cardiac diseases, including ion channelopathies (long QT and Brugada syndromes), and arrhythmogenic right ventricular cardiomyopathy, with similar observations of efficacy.¹¹⁻¹⁶

European investigators and centers have been more resistant to embracing the ICD in such diseases.^{17,18} The reasons for these disparities are multifactorial but also include the persistently lower overall implant rates in European countries compared to that in the US.^{18,19} For that reason, the multicenter report of Marin et al²⁰ in this issue of *REVISTA ESPAÑOLA DE CARDIOLOGÍA* is of particular note as the first substantial series of patients with HCM and ICDs from Spain, as well as one demonstrating the efficacy of device treatment in this disease.

SEE ARTICLE ON PAGES 537-44

Risk Stratification and Selection of Patients

The effectiveness of the ICD in HCM, by virtue of sensing and automatically terminating potentially

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lethal ventricular tachyarrhythmias, is no longer in question. Indeed, the American College of Cardiology/European Society of Cardiology consensus panel regarded the ICD as the most effective strategy for prevention of sudden death in HCM for both secondary and primary prevention.¹

However, based on a number of studies over the past 5 years, the precise selection of those patients most likely to benefit from a prophylactic (primary prevention) ICD remains a challenge, largely due to the particularly heterogeneous clinical profile of HCM and therefore the mismatch between the power of the ICD to prevent sudden death and our ability (by virtue of risk stratification) to identify with precision those patients who would benefit most from device therapy.^{1,2,21} A number of non-invasive risk markers have been identified by virtue of retrospective observational studies for primary —i.e., family member with premature HCM-related death; syncope; particularly in the young and when exertional or multiple; nonsustained ventricular tachycardia on ambulatory Holter ECGs, when multiple, repetitive or prolonged; massive left ventricular hypertrophy with maximum wall thickness ≤ 30 mm; and hypotensive or attenuated blood pressure response to exercise.^{1,2,21-24} Left ventricular outflow obstruction is per se not generally considered a major determinant of risk for sudden death, given the particularly low positive predictive values associated with this marker, although obstruction is a strong long-term determinant of progressive heart failure.²⁵

There is little controversy in HCM regarding the appropriateness of the ICD for secondary prevention following cardiac arrest.²⁶ Indeed, Marín et al²⁰ is primarily a secondary prevention study, perhaps reflecting the less aggressive primary prevention strategies employed by some European centers. In contrast, it is the practice in the U.S. to recommend or offer the option of an ICD to HCM patients with one of the 5 primary prevention risk factors when that risk factor is judged to be major within the patient's overall clinical profile (although hypotension during exercise is rarely used solely in this clinical context). Preliminary data from the international ICD in HCM (Phase II) multicenter study²⁷ shows that 40% of patients with appropriate shocks have been implanted by their electrophysiologists after identification of only one risk factor, indicating that the high-risk HCM subset cannot be reliably identified only by the presence of multiple risk factors.

European investigators have consistently advised that at least 2 of the 5 primary prevention factors are required before a prophylactic ICD can be offered to a given patient.¹⁷ Indeed, that algorithm appears to have been followed by Marín et al,²⁰ as only 4% of their patients with an ICD had one risk factor. Furthermore, no data are provided in that paper addressing whether any patients at the participating centers had died suddenly *without* an ICD (presumably with one or zero risk markers). The “two-risk factor” model is unworkable for the U.S. electrophysiology community since this clinical algorithm does not permit the ICD to be offered as an option to all high-risk patients. This represents an obstacle to the aspiration of prevention of sudden death, and is not in the best interest of the HCM patient population with its unpredictable, electrically unstable myocardial substrate.

The multicenter, international experience with the ICD tabulated from the U.S. and several European countries (including Spain), now includes over 500 high-risk HCM patients.²⁷ Preliminary data from this large population shows that 20% of patients experienced appropriate device discharges for ventricular tachycardia/fibrillation and 60% had more than one appropriate shock. The appropriate intervention rate was 11%/year for secondary and 4%/year for primary prevention.

Also, long periods of risk are characteristic of HCM patients, who are usually young when implanted (average age, 40 years), and often with long delays between the ICD placement and the first appropriate intervention (up to 10 years in our experience). An additional treatment modality that can be utilized after an ICD is implanted for high-risk status, is a trial of dual-chamber pacing to reduce gradient in those patients with obstruction to left ventricular outflow at rest.²⁸

The mechanism and final common pathway of sudden cardiac death in HCM is ventricular tachyarrhythmia. Of note, in the study of Marín et al,²⁰ most appropriate interventions were triggered by sustained ventricular tachycardia (not ventricular fibrillation). Those purists among us would perhaps suggest that such device activation should not be regarded as truly life-saving, since it is theoretically possible for the arrhythmia to have eventually terminated spontaneously, had it not been for its interruption by the ICD. We have not taken this view

in a cardiac disease such as HCM in which there is such a substantial increase in left ventricular mass involving diseased myocardium. Furthermore, monitoring for ventricular tachycardia (with ambulatory Holter ECG) virtually always documents only very short bursts of ventricular tachycardia (typically of 3-5 beats), much shorter in duration than those which will trigger the ICD.

Conclusions

The ICD has become an important treatment option for high-risk patients with HCM. Even though the problem of sudden and unexpected death in this disease was recognized almost 50 years ago, and the ICD has been available for 25 years, it was not until only 5 years ago that defibrillator therapy was systematically promoted for HCM. The multicenter study of Marín et al²⁰ in this issue of REVISTA ESPAÑOLA DE CARDIOLOGÍA is an important contribution by demonstrating further dissemination of this treatment modality, effective in preventing sudden cardiac death, into centers throughout the world. However, greater focus on primary prevention is necessary, since this is the only meaningful strategy by which abolition of sudden death in young people with HCM can be achieved.

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